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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,390	10/25/2005	Virginie Louvain	263989US0PCT	2517

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
05/08/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/518,390	LOUVAIN ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,9,10 and 18-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,9,10 and 18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office action is in response to Applicants' remarks received February 24, 2009.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 1-2, 4-8, 11-17, 23-38 are canceled. Claims 3, 9-10, 18-22 are pending and currently under examination.

Priority: The request for priority to FRANCE 0208299, filed July 3, 2002, is acknowledged.

Objections and Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 3, 18, 22 remain rejected under 35 U.S.C. 102(e) as being anticipated by Himmelspach et al. (US 6573071; previously cited). Himmelspach et al. teach a Factor X analogue having a processing site for a protease other than trypsin, Factor IXa, Factor VIIa, said analogue comprising a Factor X amino acid sequence wherein amino acids Gly228 to Ile235 have the sequence of Gly228-R6-R5-R4-R3-R2-Arg234-R1 (col. 83, see also SEQ ID NO: 27), wherein

a) R1 is an amino acid selected from the group consisting of Ile, Val, Ser, Thr, and **Ala**,

b) R2 is an amino acid selected from the group consisting of **Pro**, Gly, Lys, and Arg,

c) R3 is an amino acid selected from the group consisting of Phe, Lys, Met, Gln, Glu, Ser, **Val**, Arg, and Pro

d) R4 is an amino acid selected from the group consisting of Asp, Ile, Ser, Met, Pro, Thr, Arg, Lys,

e) R5 is an amino acid selected from the group consisting of Asn, Lys, Ser, Glu, Ala, Gln, His, and Arg, and

f) R6 is an amino acid selected from the group consisting of Asp, Phe, Thr, Arg, Leu, and Ser.

Therefore, Himmelspach et al. teach a Factor X analogue with the sequence Gly228-R6-R5-R4-**Val232-Pro233-Arg234-Ala235-Val236-Gly237**, wherein the amino acids in bold correspond to the instant thrombin-cleavable sequence Val-Pro-Arg-Ala-Val-Gly (claim 3). Himmelspach et al. also teach a preparation comprising said Factor X analogue having a processing site as noted by the sequence noted above, therefore said preparation would be a medicinal product (col. 84 lines 60-67; claim 22).

While Himmelspach et al. do not specifically teach a Factor Xa analogue, this analogue is within the scope of Factor X analogues disclosed by Himmelspach et al. since upon cleavage of the Factor X analogue of Himmelspach et al. as noted in the paragraph above, one of ordinary skill would obtain a Factor Xa analogue (claim 18).

In their response, Applicants assert that Himmelspach et al. fail to disclose or suggest a factor X analogue having the sequence Leu-Thr-Arg-Ile-Val-Gly (instant SEQ ID NO: 1) of the activation site of native factor X replaced with the sequence Val-Pro-Arg-Ala-Val-Gly (instant SEQ ID NO: 9) with sufficient specificity and that the artisan would have no reason to select this factor X analogue from the extensive list of alternative factor X analogues, much less an expectation of the beneficial results flowing from the same. Indeed, when a compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, as in Himmelspach et al., anticipation can only be found if the classes of [possibilities] are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App & Inter. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. Typically, one of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds (or in this case, each factor X analogue) included in the generic formula before any of the compounds can be "at once envisaged." *In re Petering,* 301 F.2d 676, 133 USPQ 275 (CCPA 1962). Applicants further assert that when looking to see whether there would even be a motivation to select the specifically claimed factor X analogue, the artisan may look to the preferred analogues disclosed by Himmelspach et al. None of the preferred analogues disclosed by SEQ ID NOS: 29-74 of Himmelspach et al. comprises the specific combination wherein R1 would be Ala, R2 would be Pro, and R3 would be Val, which corresponds to the Factor X analogue of the presently claimed invention. Applicant's arguments have been fully considered but they are not persuasive.

Firstly, it should be noted that claim 3 is essentially directed to a Factor X analogue having the sequence Val-Pro-Arg-Ala-Val-Gly (instant SEQ ID NO: 9) at the activation site. On page 6, line 15, the specification discloses that the present invention is a factor X analogue having a thrombin-cleavable sequence characterized in that said thrombin-cleavable sequence is the sequence Pro-Arg-Ala. As noted in the 102(e) rejection above, Himmelspach et al. teach a Factor X analogue having a processing site for a protease that comprises instant SEQ ID NO: 9. Himmelspach et al. further teach that the processing site for a protease can be selected from Factor IIa. It is well known in the art that Factor IIa is thrombin. Therefore, it would be reasonable for one of ordinary skill in the art to see that the Himmelspach et al. does anticipate claim 3 because Himmelspach et al. teach that the modified processing site is cleavable by thrombin (Factor IIa) and that among the combinations of amino acids that can make up the processing site, the list includes the sequence of instant SEQ ID NO: 9. The artisan would have reason to select the factor X analogue comprising instant SEQ ID NO: 9 from the extensive list of alternative factor X analogues because Himmelspach et al. teach that the processing site can be for a thrombin-cleavable sequence (i.e. the processing site can be cleaved by Factor IIa).

For at least these reasons, the Himmelspach et al. reference is believed to be relevant art under 102(e).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19-21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Himmelspach et al. (US 6573071; previously cited). The teachings of Himmelspach et al. are outlined above. Himmelspach et al. further disclose nucleic acid molecules, expression vectors, and host cells that can be used to express the Factor X analogues disclosed by Himmelspach et al. (col. 17-28). Himmelspach et al. do not explicitly teach a nucleic acid molecule encoding the thrombin-cleavable sequence Val-Pro-Arg-Ala-Val-Gly.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a Factor X analogue having the thrombin-cleavable sequence Val-Pro-Arg-Ala-Val-Gly as disclosed by Himmelspach et al. by constructing expression plasmids for the preparation of Factor X analogue for expression in host cells (claims 19-21). The motivation to do so is given by Himmelspach et al., which disclose that Factor X analogues having the thrombin-cleavable sequence Val-Pro-Arg-Ala-Val-Gly can be prepared by constructing expression plasmids followed by transformation into a host cell for expressing a Factor X analogue protein.

The Himmelspach et al. reference is still maintained over claims 19-21 because it is believed to be relevant art for the reasons as noted above.

Claims 9-10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Himmelspach et al. (US 6573071; previously cited). The teachings of Himmelspach et al. are outlined above. Himmelspach et al. further disclose Factor X/Xa is an important component of the prothrombinase complex and may be used to treat patient suffering from blood coagulation

disorders, i.e. hemophilia (col. 3-4). Himmelspach et al. do not explicitly teach a preparation comprising a Factor X analogue with the thrombin-cleavable sequence Val-Pro-Arg-Ala-Val-Gly and a method of treating hemophilia utilizing said Factor X analogue.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the Factor X analogue of Hammelspach et al. to a patient for the treatment of hemophilia because Hammelspach et al. disclose Factor X/Xa which exhibits high stability and can be activated to Factor Xa without use of conventional proteases (col. 4 lines 30-35), i.e. modified to have the thrombin-cleavable sequence Val-Pro-Arg-Ala-Val-Gly, can be administered to treat patients suffering from hemophilia (claims 9-10).

The Himmelspach et al. reference is still maintained over claims 9-10 because it is believed to be relevant art for the reasons as noted above.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

April 29, 2009